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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/085,239	WARD ET AL.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-51* is/are rejected.

7)☒ Claim(s) *40-41,43-45,47* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 40-51 are presented for examination.

A request for continued examination under 37 C.F.R. 1.114, including the fee set forth in 37 C.F.R. 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 C.F.R. 1.114, and the fee set forth in 37 C.F.R. 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 C.F.R. 1.114. Applicant's payment and submission filed July 11, 2008 has been received and entered into the present application. Accordingly, prosecution has been reopened.

Claims 40-51 remain pending and under examination. All claims are amended.

Applicant's arguments, filed July 11, 2008, have been fully considered. Rejections and objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set of rejections and objections presently being applied to the instant application.

Objections to the Claims (New Grounds of Objection)

Claims 40-41, 43-45 and 47 are objected to for failing to recite proper Markush language. In particular, the claim recites, "selected from the group comprising…". Proper Markush construction requires the transitional language to read "selected from the group consisting of A, B and C". Please reference MPEP §2173.05(h)(I) for clarification of Markush limitations.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40-51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In particular, the antecedent basis for the phrase "in need thereof" as recited in independent claims 40-42, 44-46 and 48-50 is unclear because the claims do not specifically set forth whether the phrase "in need thereof" limits the patients to be treated to (1) those that are in need of treatment of a hyperproliferative disease of the skin or (2) those that are in need of the pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway, which is carbenoxolone, and is in combination with one or more pharmaceutically acceptable carriers, diluents or excipients. For this reason, the claims fail to clearly, deliberately and precisely set forth the patient that is to be treated in the instantly claimed methods. Accordingly, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the scope of the subject matter for which Applicant is presently seeking protection.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

For the purposes of examination, the claims will be interpreted to read upon the treatment of any patient that is in need of the instantly claimed pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway, which is carbenoxolone, and is in combination with one or more pharmaceutically acceptable carriers, diluents or excipients.

Claim Rejections - 35 USC § 102 (New Grounds of Rejection)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 40-43 and 48-51 are rejected under 35 U.S.C. 102(b) as being anticipated by Gottfried et al. (GB 2023001 A; 1979).

Gottfried et al. teaches pharmaceutical compositions for treating, alleviating and ameliorating the symptoms of cancer in humans that comprise at least one glycyrrhetinic acid derivative compound or a pharmaceutically compatible salt thereof in admixture with a pharmaceutical diluent or carrier (abstract), wherein the compound is, *inter alia*, glycyrrhetinic acid hemisuccinate (also known as carbenoxolone sodium; p.2, l.7-11). Gottfried et al. discloses that the compositions may be administered orally, rectally, vaginally or by injection for the treatment of neoplasms and various forms of cancer, such as, e.g., neoplastic diseases of the gastrointestinal tract, vagina, uterus, or mammary glands (abstract; p.1, l.62-65).

For clarity of the record, though it is noted that Gottfried et al. teaches the treatment of cancer in humans and not specifically the hyperproliferative skin diseases of instant claims 41-43 or 49-51 (e.g., psoriasis, acne vulgaris, hyperkeratosis, Darier's disease, etc.), the patient to be treated by said claims is a "patient in need thereof". As explained *supra*, the claims as presently written fail to clearly set forth whether such a patient is (1) in need of treatment of a hyperproliferative skin disease or (2) in need of treatment with the instantly claimed pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway. Accordingly, the claims reasonably read upon the treatment of a patient in need of treatment with the claimed pharmaceutical composition, which is clearly met by the teachings of Gottfried et al. as discussed *supra*.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 40-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burchardt et al. (WO 97/15298; 1997), already of record, for the reasons of record set forth at pages 4-11 of the previous Office Action dated January 11, 2008, of which said reasons are herein incorporated by reference.

Newly amended claims 40-51 are properly included in the present rejection because Burchardt et al. teaches the treatment of acute and chronic inflammatory disorders, such as psoriasis (p.6, l.1-11), using a glucocorticosteroid, of which carbenoxolone sodium is specifically named, and an LTD4 receptor antagonist (p.1, l.4-6 and p.2, l.3-7). Burchardt et al. expressly discloses that the combination can be used topically as an ointment or cream for application to the skin (p.6, l.18-20). Applicant's amended claims are directed to (1) a method of treating a hyperproliferative disease of the skin subject to treatment by inhibition of the retinoic acid biosynthetic pathway, wherein the disease is, *inter alia*, psoriasis, consisting of administering a pharmaceutical composition to a patient in need thereof, wherein the pharmaceutical composition consists of a single inhibitor of the retinoic acid biosynthetic pathway which is carbenoxolone and one or more pharmaceutically acceptable carriers, diluents or excipients (claims 40-42 and 48-50) or (2) a method of treating a hyperproliferative disease of the skin subject to treatment by inhibition of the retinoic acid biosynthetic pathway, wherein the disease is, *inter alia*, psoriasis, by topically administering to skin that is to be treated of a patient in need thereof, a pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway, which is

carbenoxolone and one or more pharmaceutically acceptable carriers, diluents or excipients, wherein the instant specification defines a pharmaceutically acceptable carrier as "being compatible with the other ingredients in the formulation and not injurious to the patient" and that it should be "biologically acceptable without eliciting an adverse reaction (e.g., immune response) when administered to the host" (p.71, l.15-18). In light of such a definition, the LTD4 receptor antagonist of Burchardt et al. meets Applicant's limitation directed to a "pharmaceutically acceptable carrier" because (1) it is clearly compatible with the other agents in the formulation and (2) is also clearly not injurious to the subject to be treated, since it is formulated specifically for pharmaceutical use. Accordingly, Burchardt et al. provides for the (topical) administration of a composition consisting of carbenoxolone (i.e., the inhibitor of the retinoic acid biosynthetic pathway as instantly claimed) with an LTD4 receptor antagonist (considered, in this case, to be equivalent to the "carrier" of Applicant's amended claims) to a subject (or the affected skin of said subject) in need of treatment of psoriasis, which meets Applicant's limitations of claims 40-42, 44-46 and 48-50.

Furthermore, for clarity of the record, though it is noted that Burchardt et al. teaches the treatment of psoriasis in humans and not specifically the skin disease of instant claims 43, 47 or 51 (e.g., Darier's disease), the patient to be treated by said claims is a "patient in need thereof". As explained *supra*, the claims as presently written fail to clearly set forth whether such a patient is (1) in need of treatment of said skin disease or (2) in need of treatment with the instantly claimed pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway. Accordingly, the claims reasonably read upon the treatment of a patient in need of treatment with the claimed pharmaceutical composition, which is clearly met by the teachings of Burchardt et al. as discussed *supra*.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the claimed invention relates to the use of

carbenoxolone as the active ingredient and excludes the use of any other inhibitors. Applicant further submits that Burchardt et al. fails to teach or suggest each and every element of the invention because the reference teaches the use of carbenoxolone sodium *and* an LTD4 receptor antagonist, not carbenoxolone alone as instantly claimed. Applicant asserts that the use of the LTD4 receptor antagonist as taught by Burchardt et al. constitutes a teaching away from the use of carbenoxolone alone.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Though the claims as amended are limited to the administration of carbenoxolone and one or more pharmaceutically acceptable carriers, diluents or excipients, Applicant defines the term "pharmaceutically acceptable carrier" as a carrier that is "compatible with the other ingredients in the formulation and not injurious to the patient" and that it should be "biologically acceptable without eliciting an adverse reaction (e.g., immune response) when administered to the host" (p.71, l.15-18) and provides exemplary carriers that may be used at p.71, l.11-18 of the instant specification. In light of such a definition, the LTD4 receptor antagonist of Burchardt et al. meets Applicant's limitation directed to a "pharmaceutically acceptable carrier" because (1) it is clearly compatible with the other agents in the formulation and (2) is also clearly not injurious to the subject to be treated, since it is formulated specifically for pharmaceutical use.

Accordingly, because Burchardt et al. clearly provides for the (topical) administration of a pharmaceutical composition that is limited to a glucocorticosteroid (i.e., carbenoxolone) in combination with an LTD4 receptor antagonist to a subject (or affected skin of a subject) suffering from psoriasis for the treatment of psoriasis, and the LTD4 receptor antagonist meets Applicant's limitation of "one or more pharmaceutically acceptable carriers" as described *supra*, the teachings of Burchardt et al. continue to render the instantly claimed subject matter obvious.

Applicant is reminded that the definition of a "pharmaceutically acceptable carrier" in the instant specification is non-limiting and exemplary and does not preclude the use of the LTD4 receptor

antagonist compound of Burchardt et al. as the "carrier" of the disclosed composition. As a result, Applicant's claims, in fact, do *not* preclude the administration of another agent as alleged by Applicant, so long as it is (1) compatible with the active ingredient of the formulation and (2) not injurious to the subject to be treated, of which the LTD4 receptor antagonist meets both criteria. Moreover, Applicant fails to point to any evidence or provide any reasoning to support the assertion that the term "one or more pharmaceutically acceptable carriers, diluents or excipients" explicitly excludes the use of the LTD4 receptor antagonist of Burchardt et al. Accordingly, it is again maintained that Applicant's proffered remarks regarding a lack of teaching in Burchardt et al. to administer the claimed carbenoxolone compound *alone* for the treatment of psoriasis in a subject in need of thereof are unpersuasive in view of the fact that Applicant's instant claims fail to clearly and explicitly preclude the administration of another agent as the "carrier" to be used in combination with the active carbenoxolone compound.

For these reasons, and those previously made of record at pages 4-11 of the previous Office Action dated January 11, 2008, rejection of claims 40-51 is proper and is **maintained**.

Conclusion

The prior art made of record and not relied upon is considered pertinent to Applicant's disclosure. Please reference the publication to Kelloff et al. ("Chemopreventive Drug Development: Perspectives and Progress", *Cancer Epidemiology, Biomarkers and Prevention*, 3, 1994; 85-98).

Rejection of claims 40-51 is proper.

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

October 14, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614